ATTACHMENT B

Amendments to the Specification

Please replace the paragraph at page 1, lines 5-12 with the following amended paragraph.

The present invention relates to a laser scanning confocal microscope with fibre bundle return, for, [[-]] in particular, [[-]] improving the optical performance of laser scanning confocal microscopes. The invention may also have application in the miniaturisation of confocal endomicroscopes, in devices such as well plate readers, DNA chip scanners, in remote spectroscopy and as an optical system for a laser scanning ophthalmoscope.

Please replace the paragraph at (amended sheet) page 1, lines 15-21 with the following amended paragraph.

Existing two fibre confocal microscopes and endoscopes typically require ~~either~~ precise fibre positioning and alignment in the probe head to provide separation of the light path. Existing systems also commonly require an extended beam path or further beam compressor optics in the microscope or endoscope head to give variable pinhole capability.

Please replace the paragraphs from page 1, line 24 to (amended sheet) page 2, line 22 with the following amended paragraphs.

The present invention provides a confocal microscope or endoscope, having:

a source of coherent light for illumination of a sample;

a light focusser for receiving and focussing said coherent light to an illumination volume that in use intersects said sample;

a beam-splitter for receiving return light returned from said sample in response to said illumination and for diverging from said return light a fluorescent component of said return light; and

an imaging optical fibre bundle ~~for receiving~~ comprising a plurality of individual fibres, having an entry end located to receive said diverged fluorescent component of said return light so that said diverged fluorescent component is transmitted to an exit end of said fibre bundle;

wherein said fibre bundle ~~provides a return channel for fluorescent return light~~ preserves, between said entry end and said exit end of said fibre bundle, the relative spatial coordinates of the cores of said individual fibres.

~~Thus, a return channel is provided that can be made optically independent and isolated from the laser delivery fibre fluorescence (and therefore decrease optical noise). The optical fibre bundle, being intended for imaging purposes, preserves, in a comparison of the entry and~~

~~relative spatial coordinates of the cores of said individual fibres.~~

Thus, a return channel is provided that can be made optically independent and isolated from the laser delivery fibre fluorescence (and therefore decrease optical noise). The optical fibre bundle, being intended for imaging purposes, preserves, [[-]] in a comparison of the entry and exit ends of the bundle, [[-]] the relative spatial coordinates of the cores of the individual fibres. Within this constraint, however, it is acceptable to transform these coordinates between the ends provided an image can still be formed. Thus, for example, the coordinates could be reversed so that a mirror image is formed. Other transformations, as will be apparent to those skilled in this art, are also possible. This constraint (i.e. that an image can be formed) means that the bundle might be termed 'coherent' in the sense that the fibre bundle maintains image orientation; this should not be confused with the coherence of the light from the light source, which refers to the maintenance of light propagation properties within the illuminating fibre.

Please replace the paragraph at page 6, lines 6-8 with the following amended paragraph.

Figure 10 is a schematic representation of a photograph of the exit end of a fibre optic bundle for use with the laser scanning confocal microscope of figure 2.

Please replace the paragraph at page 8, lines 23-37 with the following amended paragraph.

In Figure 2 a laser 42 provides a beam of TEMoo light 44, which is focussed by focussing lens 46 to the tip 48 of a single mode optic fibre 50. The light travels along the fibre core and emerges from the fibre tip 52 as a divergent beam 54. The light is collimated by collimating lens

56 to form a beam 58 that passes though a glass prism 60 from which it emerges as beam 62. Passing through the prism does not change the beam, as the light is monochromatic. The beam 62 is then deflected as an acquisition raster by the XY scanner 64. The scanned beam 66 is then focussed by focussing lens 68 through tissue sample 70 to a focussed spot 72. The reflected and fluorescent light from this spot retraces the same general set of ray paths back through focussing lens 68, is descanned by the XY scanner 64 and travels along beam path 62 to prism 60.

Please replace the paragraph at page 9, lines 15-31 with the following amended paragraph.

The beam 78 passes through collimating lens 56 and is focussed onto the polished end 80 of a 'coherent' (i.e. an image orientation maintaining) fibre optic bundle 82. The fluorescence is broad banded, that is, it consists of a range of wavelengths. Hence it is actually focussed as a spectral line on the end 80 of the bundle 82, which is transmitted by the 'coherent' array of fibres constituting the bundle 82 to an image 84 on the exit end 86 of the bundle 82. A lens 88 projects a magnified image 90 in space of the line 84 and the fibre bundle 82. The light forming this image 90 continues on to impinge on the photomultiplier tube 92 and generates an electrical signal, which forms the image. A pair of adjustable jaws 94 and 96 are provided which form a slit in width to allow a selected fraction of the near confocal fluorescent light to pass to the photomultiplier tube 92, so that the depth of field isolation can be controlled.

Please replace the paragraph at page 10, lines 18-33 with the following amended paragraph.

Figure 3D depicts a variation of the arrangement of figure 3A, and shows the end of the fibres in the microscope head. The confocal collection fibres 100 of the bundle 82 again collect light along the spectral line 103. However, in this variation the delivery fibre 50 has one side 108 ground flat towards the core 102. This brings the point from which light is emitted (i.e. the core 102) closer to the cores of the fibre bundle 82, which minimizes "spot wander" (defined below) with fibre tip scanning. It also allows imaging to be carried out using fluorescence, which is closer in wavelength to the excitation wavelength. In this embodiment, the shape of the bundle could also be altered so that the core 102 of fibre 50 is still closer - or even within - the bundle 82, reducing or eliminating the amount of divergence that is required to be provided by prism 60.

Please replace the paragraph at page 12, line 10 to page 13, line 4 with the following amended paragraph.

Light generated by fluorescence at the focal volume also retraces the same general set of ray paths as the reflected light until it reaches the prism 128. Fluorescence is always of a longer wavelength than the excitation wavelength, so the fluorescent light is deflected by a smaller angle on passing through the prism than the reflected excitation light and it forms a beam 146. This beam 146 passes through collimating lens 124 and is focussed onto the polished end 148 of a 'coherent' (i.e. image orientation maintaining) fibre optic bundle 150. The fluorescence is broad banded, that is, it consists of a range of wavelengths. Hence it is actually focussed as a spectral line 152 on the end of the bundle. This is transmitted by the 'coherent' array of fibres to form an image of the line 154 at the exit end 156 of the bundle 150. A lens 158 is situated optically after the exit end 156 of the bundle 150, the distance 160 between the exit end 156 and the lens 158 being the focal length of the lens 158. Light from the green end 162 of the spectral line 154 (i.e. green fluorescence from blue light excitation) emerges from the fibre bundle and is collimated as beam 166. Light from the red end 164 of the fluorescence spectral line is also collimated as a beam 168. The green collimated beam and the red collimated beam are at an angle to one another but, when they pass through a second prism 170, the green beam is refracted by a greater angle and both beams end up travelling parallel to one another. Thus when they enter an achromatic lens 172 they all are focussed to a single diffraction limited spot 174, which passes through the central aperture of an iris diaphragm 176 and impinges on a photomultiplier tube 178 to produce the electrical signal.

Please replace the paragraph at page 14, lines 25-29 with the following amended paragraph.

Fortunately there are a number of ways of minimising or eliminating these problems. Listed below are a number of methods that can do can this, however, it is possible that there may be further ways that could also work just as well.

Please replace the paragraph at page 15, lines 6-13 with the following amended paragraph.

In general both effects can be minimised (and possibly made insignificant) by designing the scanning optics so that the laser emission fibre tip is brought as close as possible to the tip of the fibre bundle, (still being coplanar with the flat polished tip). This can be achieved by ~~polished~~ polishing down one side of the cladding of the laser emitting fibre (as in Figure 3D) or by etching down the cladding using an ammonium bifluoride solution.

Please replace the paragraph/sub-heading at page 15, lines 32-33 with the following amended (to add underlining thereto - thus the double underlining representing underlining added and underlining thereof showing that underlining was added) paragraph/sub-heading.

Optical Design Producing Spectral Separation of Two or More Channels of Fluorescence

Please replace the paragraph/sub-heading at page 16, lines 13-14 with the following amended (to add underlining thereto - thus the double underlining representing underlining added and underlining thereof showing that underlining was added) paragraph/sub-heading.

Scanning in Remote Fluorescence Spectroscopy and Gene Chip Readers

Please replace the paragraph at page 20, lines 4-6 with the following amended paragraph.

An alternative possibility is for the fibre bundle in the head to be moved by the slow scanning mechanism but not to be moved by the fast scan mechanism.

Please replace the paragraph at page 25, lines 19-30 with the following amended paragraph.

In figure 9 the fibre 322, fibre bundle 324, collimating lens 326 and the prism 328 are held on a rigid mount 330, which is attached to the frame 332 of the endomicroscope head by two flexible strips of metal (flexure strips 318 and 320). Slow scanning motion is provided by actuator 344[[334]]. The unequal lengths of the two metal strips 318 and 320 cause the mount 330 to rotate as it moves away from the frame of the endomicroscope assembly. This rotation is centred on the back focal plane of the image-producing lens 336 or, more precisely, on the reflected

position of the back focal plane as imaged in a mirror 338 which is used in resonant fast scan mode.

Please replace the paragraph at page 26, lines 13-22 with the following amended paragraph.

Figure 10 is a schematic representation 350 of a photograph of the exit end 86 of a fibre optic bundle 82 for use with the scanning confocal microscope with fibre bundle return of figure 2. The photograph was taken with an Olympus (TM) brand SZ microscope; and the diameter 352 of the outer casing ~~(1.5 mm)~~ is 1500±100 μm and the diameter of individual fibres is ~~(~~7.0±0.5 μm - see insert 356 of portion 358~~) are indicated~~. The illuminated line 354 (from red end 360 to green end 362) is the image of dispersed fluorescence through a direct vision prism; the insert 356 is an enlarged view of a partly illuminated portion of the individual fibre tips.